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Remarks

Claims 1-9 and 14-18 remain in this application. Claims 1-3, 9, and 17 have been amended.

Elections/Restrictions

Applicants affirm election of group I, claims 1-9 and 14-18.

Objections

Claim 9 was objected to as containing a language informality. Applicant has amended claim 9 pursuant to the Examiner's suggestion.

Rejection of Claims 1-9 and 14-18 Under 35 USC Section 112, Second Paragraph

The Examiner alleges that claims 1-9 and 14-18 are indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. With respect to claims 1-3, the Examiner states, "it is unclear what is contemplated by 'the cancer comprises a carcinoma'".

The terms "cancer" and "carcinoma" are well known in the medical arts. Merriam Webster's Medical Desk Dictionary defines "cancer" as "a malignant tumor of potentially unlimited growth that expands locally by invasion and systemically by metastasis"; it defines "carcinoma" as "a malignant tumor of epithelial origin." Applicant describes these terms in the specification, "cancer" as "any cellular tumor, or mass, that, when not treated, grows" (page 7), and "carcinoma" as "any cancer that arises from epithelial tissue" (page 7). Thus, there would be no ambiguity as to the meaning of these terms.

With respect to Claim 2, the Examiner objected to use of "comprising" in association with "cancer" and "carcinoma." Applicant has amended claim 2 to specify that the cancer is a carcinoma.

Claim 17 has been amended pursuant to the Examiner's suggestion to remove a typographical error specifically by deleting the phrase "in a daily dose of" which was inadvertently repeated twice in the original claim.

Claim 18 was rejected on the alleged ground that "it is unclear what is meant by 'further administering calcium, vitamin D, or a combination thereof'." Claim 18 depends from claim 1 which is directed at reducing the risk of cancer by administering an effective amount of PTH. Claim 18 adds a limitation that the method comprise the

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administration of calcium and/or vitamin D. Applicant respectfully asserts that the meaning of claim 18 would be clear to the skilled artisan, and therefore that the requirements of Section 112, second paragraph have been met.

Rejection of Claims 1-9 and 14-17 under 35 USC Section 102

The Examiner rejected claims 1-9 and 14-17 for alleged anticipation over WO 92/00753 (The Regents of the University of California; hereinafter "Regents"); Aiginger et al. (hereinafter "Aiginger"); Trembling et al. (hereinafter "Trembling"); and Holick.

The law on anticipation requires that a single prior art reference disclose each and every element of the claimed invention, expressly or inherently.

Regents (WO 92/00753)

The Examiner states, "WO 92/00753 teaches the use of PTH for the treating cancer in humans [i.e. reducing risk of cancer](abstract, claims 1, 27-20)." Applicant respectfully disagrees.

Regents discloses use of *analogs* of PTH and PTHrP. For example, the abstract states, "the serine amino acid at position 3, the glutamine amino acid at position 6, the histidine amino acid at position 9 or combinations thereof are substituted by other natural or synthetic amino acids." Claim 1 of Regents states; "... when group B is L-serine, and J is L-glutamine, group X is not L-histidine, when group B is L-serine, and group X is L-histidine, group J is not L-glutamine, and when group J is L-glutamine and group X histidine, group is not L-serine." This proviso clearly excludes the native PTH sequence. As such Regents does not disclose Applicant's claimed invention, which relates to use of PTH or fragments thereof.

Aiginger

The Examiner states, "Aiginger teach [sic] the use of PTH to treat carcinoma, such as breast, prostate, and bone [i.e. reducing risk of cancer](abstract)". Applicant respectfully challenges the allegation that Aiginger teaches Applicant's claimed invention.

Applicant claims use of PTH for "reducing the risk of cancer." Aiginger does not teach this. It is noted from the abstract that Aiginger relates to use of PTH *in combination* with "radiophosphorus for therapy of multiple bone metastases." Aiginger

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does not mention use of PTH for "reducing the risk of cancer." Indeed all 7 of Aiginger's patients *had* carcinoma of the breast or prostate and multiple bone metastases. Thus, Aiginger relates to *treatment* of cancer and not to *reducing the risk* of getting cancer.

Trembling

The Examiner states, "Trembling et al. teach the use of PTHrP (PTH related protein) 1-34 to inhibit the proliferation of breast cancer cell lines [i.e. reducing risk of cancer](abstract)." Applicant respectfully traverses this rejection.

Applicant notes that Trembling does not disclose use of PTH to reduce the risk of cancer. Rather, Trembling discloses the effects of PTHrP 1-34 and PTH 1-34 on proliferation of breast cancer cells in culture. As such, Trembling does not anticipate the claimed invention.

Holick

The Examiner states, "Holick teaches the use of human PTH or fragments thereof (e.g. PTH(1-34)) in the treatment of cancer, by the inhibition of cancer cell proliferation and by the induction of differentiation [i.e. reducing risk of cancer](see column 4, lines 9-14; column 10, lines 27-32; and column 12, lines 12-20). Applicant respectfully traverses.

Holick does not teach use of PTH *to reduce the risk of cancer* in humans. Holick merely asserts that one or more fragments of PTH would inhibit proliferation of skin cells in culture and induce differentiation *in vitro*. There is no teaching or suggestion in Holick that PTH would be useful in reducing the risk of cancer. To state that some agent may be useful in *treating* a disease is not the same as asserting it reduces the risk of getting the disease. Holick does not show a link, nor does any other reference to which Applicant is aware. As such, Holick does not anticipate the claimed invention.

Rejection of Claims 1-9 and 14-18 under 35 USC Section 103

Claims 1-9 and 14-18 were rejected allegedly as being obvious over Regents, Aiginger, Trembling, and Holick in view of Bishop et al (US 5,972,917; hereinafter "Bishop"). The Examiner states that Regents, Aiginger, Trembling, and Holick fail to teach "the additional use of Vitamin D or calcium with PTH in reducing the risk of cancer." However, the Examiner notes, "Bishop et al. teach the use of Vitamin D and a calcium receptor agonist [i.e. calcium] in a method of achieving an effect in a

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patient to alleviate the pathological effects of cancer such as skin, breast colon, and prostate (claims 1, 10, and 15)." Applicant respectfully traverses.

The Patent Office has the burden of establishing a *prima facie* case of obviousness. *In re Oetiker*, 24 USPQ2d 1443 (Fed. Cir. 1992) (When obviousness is at issue, the examiner has the burden of persuasion and therefore the initial burden of production. Satisfying the burden of production, and thus initially, the burden of persuasion, constitutes the so-called *prima facie* showing). A showing of *prima facie* obviousness requires that (1) prior art must disclose or suggest the modification that is required for arriving at the invention, and (2) prior art must convey to one skilled in the art a reasonable expectation of success if the modification is made. See *In re Vaack*, 20 USPQ2d 1438 (Fed. Cir. 1991).

As argued in the preceding section, Regents, Aiginger, Trembling, and Holick all fail to teach use of PTH for *reducing the risk* of cancer. The same holds for Bishop. The Examiner asserts:

Bishop et al. teach the use of Vitamin D and a calcium receptor agonist (i.e. calcium] in a method of achieving an effect in a patient to alleviate the pathological effects of cancer such as skin, breast colon, and prostate (claims 1, 10, and 15). It would have been obvious . . . to use Vitamin D and calcium (if intended in a method of reducing the risk of cancer) in the methods of any of WO 92/00753, Aiginger et al, Trembling et al, and Holick because Bishop et al. teach the advantageous use of Vitamin D and calcium in a method directed to reducing the effects of cancer.

The Examiner's statement does not establish a *prima facie* case. Firstly, the Examiner has not established basis for a motivation to combine the references cited, nor that in the event such basis were present that the combination would suggest the claimed invention. Secondly, Regents, Aiginger, and Trembling all relate to *analogs* of PTH or PTHrP and not to PTH *per se* or fragments thereof. Indeed, Trembling indicated that PTH(1-34) was *ineffective* in inhibiting the proliferation *in vitro* of breast cancer cells whilst PTHrP(1-34) was effective. Thus, if anything the cited art would have taught away from the claimed invention.

An additional argument for patentability is that the references cited are limited to use of agents that might be useful in *treating* cancer. There is not the slightest suggestion in any of the cited references that PTH would be effective in *reducing the risk*

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of getting cancer. Treating a disease and reducing the risk of getting the disease are two entirely different matters. Applicant does not claim use of PTH to treat cancer; Applicant claims use of PTH to reduce the risk of getting cancer.

Applicant respectfully submits that each point of the rejection has been adequately addressed, and request the case be passed to issuance.

Respectfully submitted,



Thomas D. Webster, PhD
Attorney for Applicant
Registration No. 39,872
Phone: 317-276-3334

Eli Lilly and Company
Patent Division/TDW
P.O. Box 6288
Indianapolis, Indiana 46206-6288

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